UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/814,633	04/01/2004	Van Hung Truong	2201.0020000/RWE	7438

26111 7590 04/19/2006

STERNE, KESSLER, GOLDSTEIN & FOX PLLC
1100 NEW YORK AVENUE, N.W.
WASHINGTON, DC 20005

EXAMINER	
GRAFFEO, MICHEL	

ART UNIT	PAPER NUMBER
1614	

DATE MAILED: 04/19/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/814,633	TRUONG, VAN HUNG	
	Examiner	Art Unit	
	Michel Graffeo	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12 and 19-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12 and 19-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1 Sept 05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-12 and 19-21, drawn to a formulation comprising methacholine chloride, classified in class 514, subclass 788.

II. Claims 13-18, drawn to a method of making a formulation comprising methacholine chloride, classified in class 514, subclass 788.

III. Claim 22, drawn to a method of performing bronchoprovocation, classified in class 514, subclass 826.

IV. Claims 23-26, drawn to a method for determining the amount of methacholine chloride in a sample, classified in class 424, subclass 436.

Inventions I and II are related as process of making and product made. The inventions are distinct if either or both of the following can be shown: (1) that the process as claimed can be used to make another and materially different product or (2) that the product as claimed can be made by another and materially different process (MPEP § 806.05(f)). In the instant case the product can be made by a different process which includes steam sterilization instead of filter sterilization.

Inventions I and III are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the

process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product. See MPEP § 806.05(h). In the instant case, the methacholine can be used to treat Riley-Day disease (see US Patent No. 5,352,698 to Santini) or to stimulate muscle contractions (see US Patent No. 4,163,063 to Cannon et al.).

Inventions I and IV are directed to related and are patentably distinct. The related inventions are distinct if the inventions as claimed do not overlap in scope, i.e., are mutually exclusive; the inventions as claimed are not obvious variants; and the inventions as claimed are either not capable of use together or can have a materially different design, mode of operation, function, or effect. See MPEP § 806.05(j). In the instant case, formulation which can be for a number of treatments for example has a different utility, regime strategy and classification as well as would require a separate search than an assaying method to determine sample content thereby categorizing the Inventions as having separate status in the art.

Inventions II and III are directed to related and are patentably distinct. The related inventions are distinct if the inventions as claimed do not overlap in scope, i.e., are mutually exclusive; the inventions as claimed are not obvious variants; and the inventions as claimed are either not capable of use together or can have a materially different design, mode of operation, function, or effect. See MPEP § 806.05(j). In the

instant case, a method of making a formulation can not be used with a method of treatment with a formulation especially since one, the making of the formulation, needs to occur prior to the use thereof.

Inventions II and IV are directed to related and are patentably distinct. The related inventions are distinct if the inventions as claimed do not overlap in scope, i.e., are mutually exclusive; the inventions as claimed are not obvious variants; and the inventions as claimed are either not capable of use together or can have a materially different design, mode of operation, function, or effect. See MPEP § 806.05(j). In the instant case, a method of making a formulation cannot be used with a method of assaying and same would require a separate search than an assaying method to determine sample content thereby categorizing the Inventions as having separate status in the art.

Inventions III and IV are directed to related and are patentably distinct. The related inventions are distinct if the inventions as claimed do not overlap in scope, i.e., are mutually exclusive; the inventions as claimed are not obvious variants; and the inventions as claimed are either not capable of use together or can have a materially different design, mode of operation, function, or effect. See MPEP § 806.05(j). In the instant case, a method for determining a patients susceptibility to asthma for example has a different utility, regime strategy and classification as well as would require a

separate search than an assay method to determine sample content thereby categorizing the Inventions as having separate status in the art.

Pursuant to a voicemail from Robert Esmond on 28 March 2006 a provisional election was made without traverse to prosecute the invention of Group I, claims 1-12 and 19-21. Affirmation of this election must be made by applicant in replying to this Office action. Claims 13-18 and 22-26 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Status of Action

Claims 1-12 and 19-21 are pending and examined.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-3 and 5-6 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "about" in the phrases "about 4 to 5" regarding pH ranges and "about 4.5 to about 4.7" regarding concentration are relative terms which render the claims indefinite. Since the term "about" is not defined by the claims and the specification does

not provide a standard for ascertaining the requisite degree, one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

Because objective standards for the term "about" has not been provided by Applicants, subjective interpretations of these terms would be involved in determining whether or not a particular period of time or dose is included by or excluded from the present claims. It is therefore the Examiner's position that the public would not be informed of the boundaries of what constitutes infringement of the present claims and thus the claims fail to meet either the tenor or express requirements of 35 U.S.C. §112, second paragraph and are properly rejected.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-12 and 19-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Asmus et al. Stability of Frozen Methacholine Solutions in Unit-Dose Syringes for Bronchoprovocation. Chest 121:1634-1637 (May 2002) in view of Watson et al. Effect of pH on the stability of methacholine chloride in solution. Respiratory Medicine (1998) 92, 588-592 and further in view of (Website) Practical Engineering Data & Tools for Medical Device Professionals: Selecting a Sterilization method. (2001) http://www.engineeringreference.com/Sterilization/select%20sterilization.htm.

Asmus et al. teach a formulation of methacholine chloride wherein the concentration of methacholine is less than 0.25 mg/mL (in current claims 1-12 and 19-21; see Abstract), sodium chloride is used as a diluent (in current claim 9; see Abstract), the pH is from 4 to 5 (in current claims 1-3; see Abstract) wherein the reference is directed to stabilizing the solution and teaches that the pH should be slightly acid since pH levels above 6 encourage hydrolysis of the solution and loss of potency (see page 1634) as well as directed to a process of making a sterile solution (see Materials and Methods on page 1635) which are further stored in plastic syringes (in current claims 10-11 and 19-21; see Results page 1636).

Asmus et al. do not teach a methacholine solution comprising an acetate and a preservative whereby the solution is sterilized by aseptic filtration.

Watson et al. teach a methacholine chloride solution comprising sodium chloride (in current claim 9; see Introduction page 588) and acetate at a concentration of 0.02M (incurrent claims 4-6; see page 598) wherein the reference further teaches that methacholine rapidly decomposes due to hydrolysis under basic conditions (see Discussion page 591) and that being the basis of studying varying buffers and pHs which leads one of ordinary skill in the art to vary and optimize the concentration of acetate depending on the solution variables and desired resultant pH. Watson et al. also teach that phenol (considered a preservative since it is inhibiting contamination) can be added to the solutions to inhibit microbial growth (in current claim 8; see Discussion page 592) thereby encouraging sterile solutions.

The Practical Engineering reference teaches a process for sterilizing liquid products comprising aseptic processing and filtration (in current claim 7 see item 5). The reference further explains that many liquid pharmaceutical products cannot withstand thermal sterilization and that such are relegated to aseptic filtration and then filled into presterilized containers such as vials, ampules or syringes (in current claims 10-11 and 19-21; see item 5).

One of ordinary skill in the art would have been motivated to combine the above references and as combined teach the claimed invention as claimed. One of ordinary skill in the art would have been motivated to combine the above references because Asmus et al. and Watson et al. are both directed to stable solutions of methacholine. Moreover, both teach that pHs over 6.0 lead to destabilization and hydrolysis of the active agent therefore suggesting a lower pH which Watson et al. teach by adding acetate to the solution. Both Asmus et al. and Watson et al. teach sterile solutions since the solution will be inhaled by a patient which directs one of ordinary skill in the art to method of sterilization. The Practical Engineering reference specifically teaches that liquid pharmaceuticals can be sterilized by aseptic filtration since they cannot withstand thermal sterilization. Therefore, one of ordinary skill in the art would expect a successful sterilization process by employing the Practical Engineering reference. Thus, the combined references teach and make prima facie obvious how to use the claimed invention at the time that it was made.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michel Graffeo whose telephone number is 571-272-8505. The examiner can normally be reached on 9am to 5:30pm Monday to Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

4 April 2006
MG

CHRISTOPHER S. F. LOW
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

MG